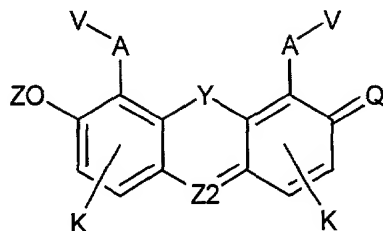


We claim:

1. A fluorescein-based ligand, comprising a ligand having the following structure:



wherein: A is a chemical moiety having one or more carbon atoms;

Z is hydrogen or any hydroxyl-protecting group;

Q is O, S or Se;

K is optionally one or more substituents of the indicated aromatic ring that do not preclude detecting a metal ion by fluorescence;

V is a chemical moiety comprising a Lewis base capable of forming one or more coordination bonds with a metal ion;

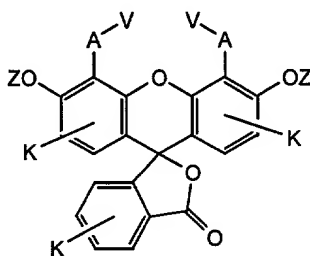
Y is O, S, Se, NR, or C(CH<sub>3</sub>)<sub>3</sub>, wherein R is an alkyl and R and the methyl groups of C(CH<sub>3</sub>)<sub>2</sub> are optionally substituted; and

Z<sub>2</sub> is N, HOOCCH<sub>2</sub>CH<sub>2</sub>C-, HOOC-CH=CH-C-, (2-carboxyphenyl)-C-, (2-sulfophenyl)-C-, (2-carboxy-3,4,5,6-tetrachlorophenyl)-C-, (2-carboxy-4-nitrophenyl)-C-, (2-carboxy-5-nitrophenyl)-C-, (2-carboxy-4-aminophenyl)-C-, (2-carboxy-5-aminophenyl)-C-, (2,4-dicarboxyphenyl)-C-, (2,5-dicarboxylphenyl)-C-, (2,4,5-tricarboxyphenyl)-C-, or other substituted (2-carboxyphenyl)-C- derivative.

2. The fluorescein-based ligand of claim 1, wherein A is one of the following: -CH<sub>2</sub>-, -C(=O)-, -C(=S)-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>C(=O)-, -CH<sub>2</sub>C(=S)-, and optionally J is substituted for any hydrogen atom of said -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>C(=O)-, or -CH<sub>2</sub>C(=S)-, wherein J is a non-interfering substituent.
3. The fluorescein-based ligand of claim 1, wherein said ligand has one or more K substituents, with each K independently being one of the following: linear or branched alkyl, alkenyl, linear or branched aminoalkyl, linear or branched

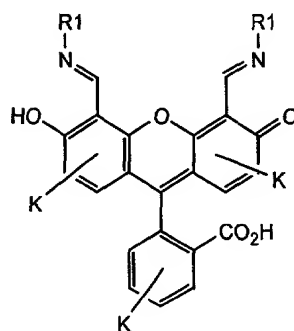
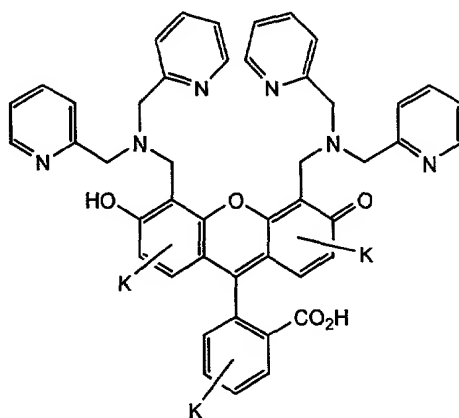
acylamino, linear or branched acyloxy, linear or branched alkoxycarbonyl, linear or branched alkoxy, linear or branched alkylaryl, linear or branched hydroxyalkyl, linear or branched thioalkyl, acyl, amino, hydroxy, thio, aryloxy, arylalkoxy, hydrogen, alkynyl, halogen, cyano, sulfhydryl, carbamoyl, nitro, trifluoromethyl, amino, thio, lower alkoxy, lower alkylthio, lower alkylamino, nitro, phenoxy, benzyloxy, hydrogen, amine, hydroxyl, alkoxyl, carbonyl, acyl, formyl or sulfonyl.

4. The fluorescein-based ligand of claim 1, wherein Q is -OZ and Z2 forms a different tautomer with the fluorescein core.
5. The fluorescein based-ligand of claim 1, wherein said ligand has the following structure:



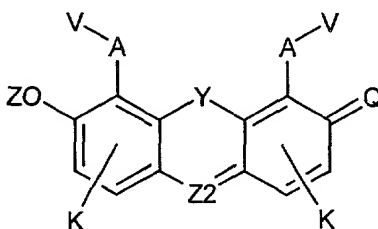
6. The fluorescein-based ligand of claim 5, wherein A is one of the following: -CH<sub>2</sub>-, -C(=O)-, -C(=S)-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>C(=O)-, -CH<sub>2</sub>C(=S)-, and optionally J is substituted for any -H of -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>C(=O)-, -CH<sub>2</sub>C(=S)-, wherein J is a non-interfering substituent.
7. The fluorescein-based ligand of claim 5, wherein said ligand has one or more K substituents, with each K independently being either -Cl or -F.
8. The fluorescein-based ligand of claim 5, wherein the fluorescein structure of said ligand is in a different isomeric form.
9. The fluorescein-based ligand of claim 1, wherein said ligand forms a chelating agent upon complexation of said ligand with a metal ion.

10. The fluorescein-based ligand of claim 9, wherein said ligand forms a tridentate or tetradentate chelating agent upon said complexation.
11. The fluorescein-based ligand of claim 1, wherein said ligand has one of the following structures:



wherein R<sup>1</sup> is aliphatic, alkyl, aralkyl, alkenyl, alkynyl, aryl or heterocyclyl, optionally substituted.

12. A fluorescein-based compound for a target, comprising the following structure:



wherein: A is a moiety having one or more carbon atoms;

Z is hydrogen or any hydroxyl-protecting group;

Q is O, S or Se;

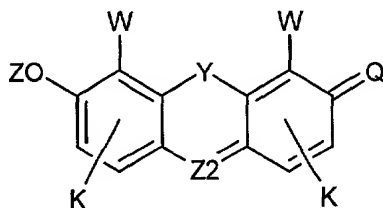
K is optionally one or more substituents of the indicated aromatic ring that that do not preclude using said compound for detecting a target;

V is a chemical moiety that may serve as a ligand to said target;

Y is O, S, Se, NR, or C(CH<sub>3</sub>)<sub>3</sub>, wherein R is an alkyl and R and the methyl groups of C(CH<sub>3</sub>)<sub>2</sub> are optionally substituted; and

Z<sub>2</sub> is N, HOOCCH<sub>2</sub>CH<sub>2</sub>C-, HOOC-CH=CH-C-, (2-carboxyphenyl)-C-, (2-sulfophenyl)-C-, (2-carboxy-3,4,5,6-tetrachlorophenyl)-C-, (2-carboxy-4-nitrophenyl)-C-, (2-carboxy-5-nitrophenyl)-C-, (2-carboxy-4-aminophenyl)-C-, (2-carboxy-5-aminophenyl)-C-, (2,4-dicarboxyphenyl)-C-, (2,5-dicarboxyphenyl)-C-, (2,4,5-tricarboxyphenyl)-C-, or other substituted (2-carboxyphenyl)-C- derivative.

13. The fluorescein-based compound of claim 12, wherein said target is a biological material.
14. The fluorescein-based compound of claim 12, wherein said target is a toxin.
15. A fluorescein-based scaffold, comprising a scaffold having the following structure:



wherein: Z is hydrogen or any hydroxyl-protecting group;

Q is O, S or Se;

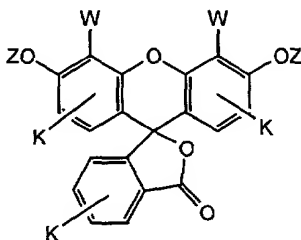
K is optionally one or more substituents of the indicated aromatic ring that do not preclude detecting a metal ion by fluorescence;

W comprises at least one carbon atom bound to the aromatic ring carbon and is a site of latent functionality;

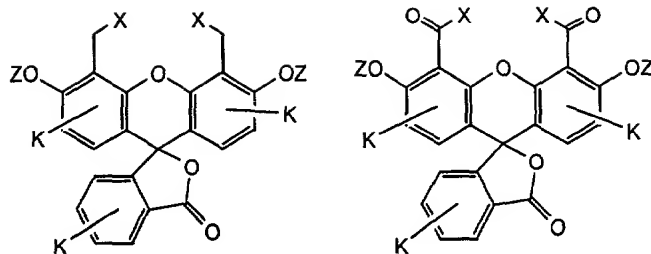
Y is O, S, Se, NR, or C(CH<sub>3</sub>)<sub>3</sub>, wherein R is an alkyl and R and the methyl groups of C(CH<sub>3</sub>)<sub>2</sub> are optionally substituted; and

Z2 is N, HOOCCH<sub>2</sub>CH<sub>2</sub>C-, HOOC-CH=CH-C-, (2-carboxyphenyl)-C-, (2-sulfohenyl)-C-, (2-carboxy-3,4,5,6-tetrachlorophenyl)-C-, (2-carboxy-4-nitrophenyl)-C-, (2-carboxy-5-nitrophenyl)-C-, (2-carboxy-4-aminophenyl)-C-, (2-carboxy-5-aminophenyl)-C-, (2,4-dicarboxyphenyl)-C-, (2,5-dicarboxylphenyl)-C-, (2,4,5-tricarboxyphenyl)-C-, or other substituted (2-carboxyphenyl)-C- derivative.

16. The fluorescein-based scaffold of claim 15, wherein said scaffold has the following structure:

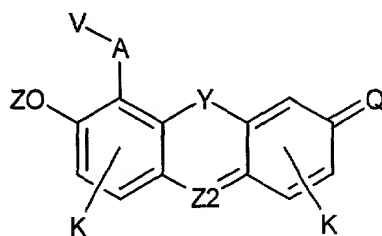


17. The fluorescein-based scaffold of claim 16, wherein W comprises one of the following: -CH<sub>2</sub>X, -C(O)H, -C(O)OR<sub>2</sub>, -C(O)OH, -C(O)X, -CN wherein X is halogen, hydroxyl, amine, thiol or other leaving group, and R<sub>2</sub> is an aliphatic, alkyl, aralkyl, alkenyl, alkynyls, aryl or heterocyclyl.
18. The fluorescein-based scaffold of claim 16, wherein the fluorescein structure of said scaffold is in a different isomeric form.
19. The fluorescein-based scaffold of claim 15, wherein said scaffold has one of the following structures:



wherein X is halogen, hydroxyl, amine, thiol or other leaving group.

20. A fluorescein-based ligand, comprising a ligand having the following structure:



wherein: A is a moiety having one or more carbon atoms;

Z is hydrogen or any hydroxyl-protecting group;

Q is O, S or Se;

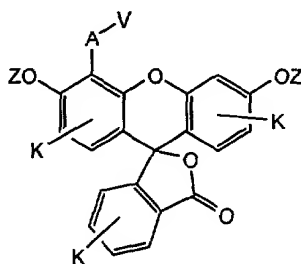
K is optionally one or more substituents of the indicated aromatic ring that do not preclude detecting a metal ion by fluorescence;

V is a chemical moiety comprising a Lewis base capable of forming one or more coordination bonds with a metal ion;

Y is O, S, Se, NR, or C(CH<sub>3</sub>)<sub>3</sub>, wherein R is an alkyl and R and the methyl groups of C(CH<sub>3</sub>)<sub>2</sub> are optionally substituted; and

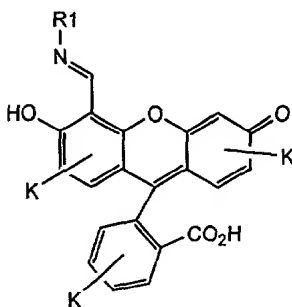
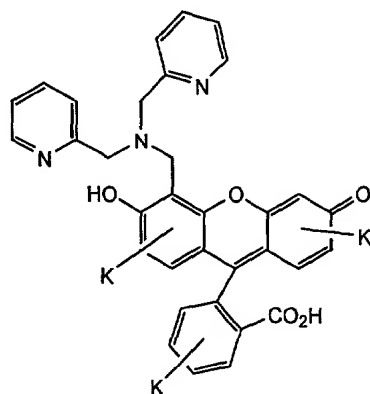
Z<sub>2</sub> is N, HOOCCH<sub>2</sub>CH<sub>2</sub>C-, HOOC-CH=CH-C-, (2-carboxyphenyl)-C-, (2-sulfohenyl)-C-, (2-carboxy-3,4,5,6-tetrachlorophenyl)-C-, (2-carboxy-4-nitrophenyl)-C-, (2-carboxy-5-nitrophenyl)-C-, (2-carboxy-4-aminophenyl)-C-, (2-carboxy-5-aminophenyl)-C-, (2,4-dicarboxyphenyl)-C-, (2,5-dicarboxyphenyl)-C-, (2,4,5-tricarboxyphenyl)-C-, or other substituted (2-carboxyphenyl)-C- derivative.

21. The fluorescein-based ligand of claim 20, wherein A is one of the following: -CH<sub>2</sub>-, -C(=O)-, -C(=S)-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>C(=O)-, -CH<sub>2</sub>C(=S)-, and optionally J is substituted for any hydrogen atom of said -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>C(=O)-, or -CH<sub>2</sub>C(=S)-, wherein J is a non-interfering substituent.
22. The fluorescein-based ligand of claim 20, wherein said ligand has one or more K substituents, with each K independently being one of the following: linear or branched alkyl, alkenyl, linear or branched aminoalkyl, linear or branched acylamino, linear or branched acyloxy, linear or branched alkoxycarbonyl, linear or branched alkoxy, linear or branched alkylaryl, linear or branched hydroxyalkyl, linear or branched thioalkyl, acyl, amino, hydroxy, thio, aryloxy, arylalkoxy, hydrogen, alkynyl, halogen, cyano, sulfhydryl, carbamoyl, nitro, trifluoromethyl, amino, thio, lower alkoxy, lower alkylthio, lower alkylamino, nitro, phenoxy, benzyloxy, hydrogen, amine, hydroxyl, alkoxyl, carbonyl, acyl, formyl or sulfonyl.
23. The fluorescein-based ligand of claim 20, wherein Q is -OZ and Z2 forms a different tautomer with the fluorescein core.
24. The fluorescein based-ligand of claim 20, wherein said ligand has the following structure:



25. The fluorescein-based ligand of claim 24, wherein A is one of the following: -CH<sub>2</sub>-, -C(=O)-, -C(=S)-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>C(=O)-, -CH<sub>2</sub>C(=S)-, and optionally J is substituted for any -H of -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>C(=O)-, -CH<sub>2</sub>C(=S)-, wherein J is a non-interfering substituent.

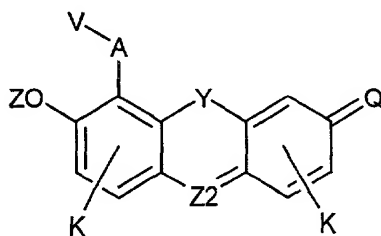
26. The fluorescein-based ligand of claim 24, wherein said ligand has one or more K substituents, with each K independently being either -Cl or -F.
27. The fluorescein-based ligand of claim 24, wherein the fluorescein structure of said ligand is in a different isomeric form.
28. The fluorescein-based ligand of claim 20, wherein said ligand forms a chelating agent upon complexation of said ligand with a metal ion.
29. The fluorescein-based ligand of claim 28, wherein said ligand forms a tridentate or tetradentate chelating agent upon said complexation.
30. The fluorescein-based ligand of claim 20, wherein said ligand has one of the following structures:



wherein R1 is aliphatic, alkyl, aralkyl, alkenyl, alkynyl, aryl or heterocyclyl, optionally substituted.



31. A fluorescein-based compound for a target, comprising the following structure:



wherein: A is a moiety having one or more carbon atoms;

Z is hydrogen or any hydroxyl-protecting group;

Q is O, S or Se;

K is optionally one or more substituents of the indicated aromatic ring that do not preclude using said compound for detecting a target;

V is a chemical moiety that may serve as a ligand to said target;

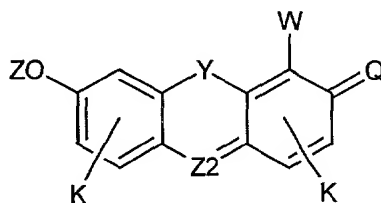
Y is O, S, Se, NR, or C(CH<sub>3</sub>)<sub>3</sub>, wherein R is an alkyl and R and the methyl groups of C(CH<sub>3</sub>)<sub>2</sub> are optionally substituted; and

Z<sub>2</sub> is N, HOOCCH<sub>2</sub>CH<sub>2</sub>C-, HOOC-CH=CH-C-, (2-carboxyphenyl)-C-, (2-sulfohenyl)-C-, (2-carboxy-3,4,5,6-tetrachlorophenyl)-C-, (2-carboxy-4-nitrophenyl)-C-, (2-carboxy-5-nitrophenyl)-C-, (2-carboxy-4-aminophenyl)-C-, (2-carboxy-5-aminophenyl)-C-, (2,4-dicarboxyphenyl)-C-, (2,5-dicarboxylphenyl)-C-, (2,4,5-tricarboxyphenyl)-C-, or other substituted (2-carboxyphenyl)-C- derivative.

32. The fluorescein-based compound of claim 31, wherein said target is a biological material.

33. The fluorescein-based compound of claim 31, wherein said target is a toxin.

34. A fluorescein-based scaffold, comprising a scaffold having the following structure:



wherein: Z is hydrogen or any hydroxyl-protecting group;

Q is O, S or Se;

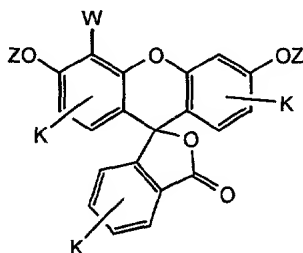
K is optionally one or more substituents of the indicated aromatic ring that do not preclude detecting a metal ion by fluorescence;

W comprises at least one carbon atom bound to the aromatic ring carbon and is a site of latent functionality;

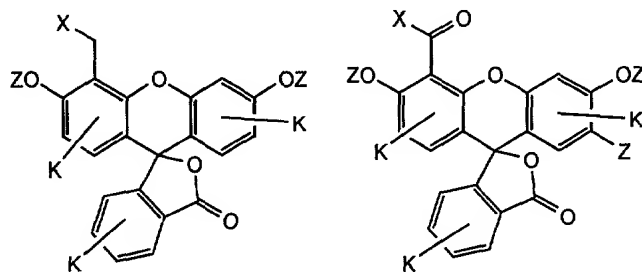
Y is O, S, Se, NR, or C(CH<sub>3</sub>)<sub>3</sub>, wherein R is an alkyl and R and the methyl groups of C(CH<sub>3</sub>)<sub>2</sub> are optionally substituted; and

Z2 is N, HOOCCH<sub>2</sub>CH<sub>2</sub>C-, HOOC-CH=CH-C-, (2-carboxyphenyl)-C-, (2-sulfophenyl)-C-, (2-carboxy-3,4,5,6-tetrachlorophenyl)-C-, (2-carboxy-4-nitrophenyl)-C-, (2-carboxy-5-nitrophenyl)-C-, (2-carboxy-4-aminophenyl)-C-, (2-carboxy-5-aminophenyl)-C-, (2,4-dicarboxyphenyl)-C-, (2,5-dicarboxylphenyl)-C-, (2,4,5-tricarboxyphenyl)-C-, or other substituted (2-carboxyphenyl)-C- derivative.

35. The fluorescein-based scaffold of claim 34, wherein said scaffold has the following structure:

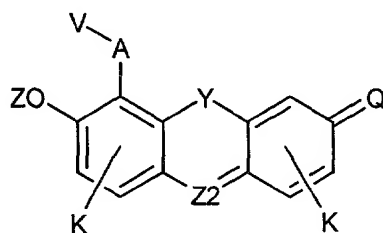
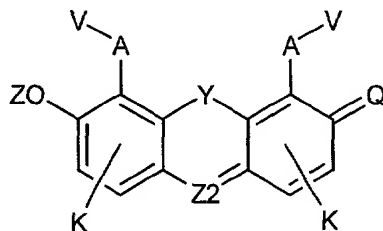


36. The fluorescein-based scaffold of claim 34, wherein W comprises one of the following: -CH<sub>2</sub>X, -C(O)H, -C(O)OR<sub>2</sub>, -C(O)OH, -C(O)X, -CN wherein X is halogen, hydroxyl, amine, thiol or other leaving group, and R<sub>2</sub> is an aliphatic, alkyl, aralkyl, alkenyl, alkynyls, aryl or heterocyclyl.
37. The fluorescein-based scaffold of claim 35, wherein the fluorescein structure of said scaffold is in a different isomeric form.
38. The fluorescein-based scaffold of claim 35, wherein said scaffold has one of the following structures:



wherein X is halogen, hydroxyl, amine, thiol or other leaving group.

39. A coordination complex, comprising a metal ion coordinated to one of the fluorescein-based ligands claimed above.
40. A coordination complex, comprising  $Zn^{2+}$  coordinated to one of the fluorescein-based ligands claimed above.
41. A method of detecting, and optionally quantifying the concentration of, a metal ion in a sample, comprising:
  - a. Adding to a sample a fluorescein-based ligand comprising one of the following structures:



wherein: A is a moiety having one or more carbon atoms;  
 Z is hydrogen or any hydroxyl-protecting group;  
 Q is O, S or Se;

K is optionally one or more substituents of the indicated aromatic ring that do not preclude detecting a metal ion by fluorescence;

V is a chemical moiety comprising a Lewis base capable of forming one or more coordination bonds with a metal ion;

Y is O, S, Se, NR, or C(CH<sub>3</sub>)<sub>3</sub>, wherein R is an alkyl and R and the methyl groups of C(CH<sub>3</sub>)<sub>2</sub> are optionally substituted; and

Z is N, HOOCCH<sub>2</sub>CH<sub>2</sub>C-, HOOC-CH=CH-C-, (2-carboxyphenyl)-C-, (2-sulfophenyl)-C-, (2-carboxy-3,4,5,6-tetrachlorophenyl)-C-, (2-carboxy-4-nitrophenyl)-C-, (2-carboxy-5-nitrophenyl)-C-, (2-carboxy-4-aminophenyl)-C-, (2-carboxy-5-aminophenyl)-C-, (2,4-dicarboxyphenyl)-C-, (2,5-dicarboxylphenyl)-C-, (2,4,5-tricarboxyphenyl)-C-, or other substituted (2-carboxyphenyl)-C- derivative; and

b. Measuring the fluorescence of said ligand in said sample; and

c. Determining whether a metal ion is present in said sample, and optionally the concentration of said metal ion in said sample.

42. The method of claim 41, wherein said sample is a cell.

43. The method of claim 41, wherein said sample is in vitro.

44. The method of claim 41, further comprising measuring the fluorescence of said ligand in said sample at a different concentration of said ligand.

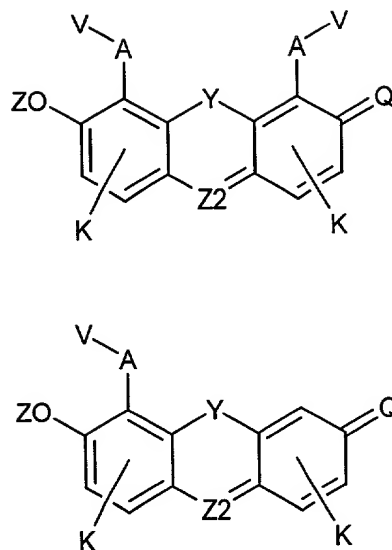
45. The method of claim 41, wherein one of said metal ions is a transition metal ion.

46. The method of claim 41, wherein one of said metal ions is Zn<sup>2+</sup>.

47. A method of detecting, and optionally quantifying the concentration of, a target in a sample, comprising:

a. Mixing with a sample a fluorescein-based compound comprising one of the following structures:

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wherein: A is a moiety having one or more carbon atoms;

Z is hydrogen or any hydroxyl-protecting group;

Q is O, S or Se;

K is optionally one or more substituents of the indicated aromatic ring that do not preclude using said compound for detecting a target;

V is a chemical moiety that may serve as a ligand to said target;

Y is O, S, Se, NR, or C(CH<sub>3</sub>)<sub>3</sub>, wherein R is an alkyl and R and the methyl groups of C(CH<sub>3</sub>)<sub>2</sub> are optionally substituted; and

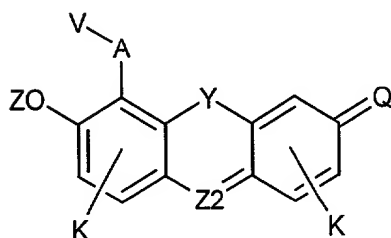
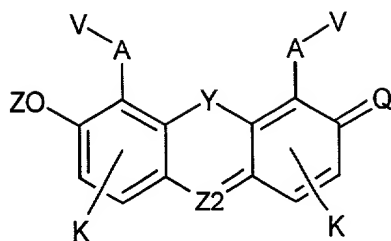
Z<sub>2</sub> is N, HOOCCH<sub>2</sub>CH<sub>2</sub>C, HOOC-CH=CH-C-, (2-carboxyphenyl)-C-, (2-sulfophenyl)-C-, (2-carboxy-3,4,5,6-tetrachlorophenyl)-C-, (2-carboxy-4-nitrophenyl)-C-, (2-carboxy-5-nitrophenyl)-C-, (2-carboxy-4-aminophenyl)-C-, (2-carboxy-5-aminophenyl)-C-, (2,4-dicarboxyphenyl)-C-, (2,5-dicarboxyphenyl)-C-, (2,4,5-tricarboxyphenyl)-C-, or other substituted (2-carboxyphenyl)-C- derivative; and

b. Measuring the fluorescence of said compound in said sample; and

c. Determining whether the target is present in said sample, and optionally the concentration of said target in said sample.

48. A diagnostic kit for a metal ion, comprising:

a. A fluorescein-based ligand comprising one of the following structures:



wherein: A is a moiety having one or more carbon atoms;

Z is hydrogen or any hydroxyl-protecting group;

Q is O, S or Se;

K is optionally one or more substituents of the indicated aromatic ring that do not preclude detecting a metal ion by fluorescence;

V is a chemical moiety comprising a Lewis base capable of forming one or more coordination bonds with a metal ion;

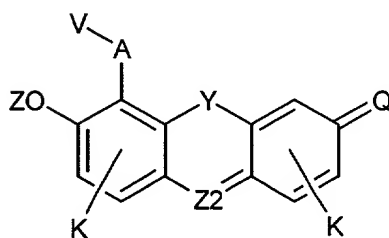
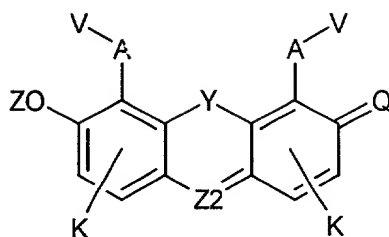
Y is O, S, Se, NR, or C(CH<sub>3</sub>)<sub>3</sub>, wherein R is an alkyl and R and the methyl groups of C(CH<sub>3</sub>)<sub>2</sub> are optionally substituted; and

Z<sub>2</sub> is N, HOOCCH<sub>2</sub>CH<sub>2</sub>C-, HOOC-CH=CH-C-, (2-carboxyphenyl)-C-, (2-sulfohenyl)-C-, (2-carboxy-3,4,5,6-tetrachlorophenyl)-C-, (2-carboxy-4-nitrophenyl)-C-, (2-carboxy-5-nitrophenyl)-C-, (2-carboxy-4-aminophenyl)-C-, (2-carboxy-5-aminophenyl)-C-, (2,4-dicarboxyphenyl)-C-, (2,5-dicarboxyphenyl)-C-, (2,4,5-tricarboxyphenyl)-C-, or other substituted (2-carboxyphenyl)-C- derivative; and

b. Instructions for using said ligand to detect a metal ion in a sample.

49. A diagnostic kit for a target, comprising:

a. A fluorescein-based compound comprising one of the following structures:



wherein: A is a moiety having one or more carbon atoms;

Z is hydrogen or any hydroxyl-protecting group;

Q is O, S or Se;

K is optionally one or more substituents of the indicated aromatic ring that that do not preclude using said compound for detecting a target;

V is a chemical moiety that may serve as a ligand to said target;

Y is O, S, Se, NR, or C(CH<sub>3</sub>)<sub>3</sub>, wherein R is an alkyl and R and the methyl groups of C(CH<sub>3</sub>)<sub>2</sub> are optionally substituted; and

Z<sub>2</sub> is N, HOOCCH<sub>2</sub>CH<sub>2</sub>C, HOOC-CH=CH-C, (2-carboxyphenyl)-C, (2-sulfophenyl)-C, (2-carboxy-3,4,5,6-tetrachlorophenyl)-C, (2-carboxy-4-nitrophenyl)-C, (2-carboxy-5-nitrophenyl)-C, (2-carboxy-4-aminophenyl)-C, (2-carboxy-5-aminophenyl)-C, (2,4-dicarboxyphenyl)-C, (2,5-dicarboxylphenyl)-C, (2,4,5-tricarboxyphenyl)C-, or other substituted (2-carboxyphenyl)-C derivative; and

b. Instructions for using said compound to detect a target in a sample.